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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/519,925 | 01/03/2005 | Tasuku Honjo | Q85588 | 9146 |

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WASHINGTON, DC 20037-3213

| EXAMINER | |
|---|---|
| OUSPENSKI, ILIA I | |

| ART UNIT | PAPER NUMBER |
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| 1644 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/519,925 | HONJO ET AL. | |
| | Examiner | Art Unit | |
| | ILIA OUSPENSKI | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *13,14 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's amendment and remarks, filed on 01/07/2008, are acknowledged.

Claims 1 – 12, and 15 – 32 have been canceled.
Claim 33 has been added.

**Claims 13, 14, and 33 are pending.**

The rejections of record can be found in the previous Office Action, mailed on 07/06/2007.

***The objections and rejections of record have been withdrawn in view of Applicant's amendment and arguments, except as set forth herein.***

2. The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

3. Claims 13 and 14 stand rejected, and newly added claim 33 is rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

The rejection of record is maintained for the reasons of record. Applicant's arguments have been fully considered but have not been found sufficiently convincing.

The instant specification discloses in Example 12 at pages 44 – 46 that anti-PD-1 antibody enhances cytotoxic activity of mouse cytotoxic T cells in vitro towards P-815 cells overexpressing PD-L1. Example 13 at page 46 discloses a working example wherein an anti-PD-1 antibody administered to mice injected with B16 melanoma cells reduced the liver weight, which is interpreted as indicative of suppressing metastases to the liver. When considered together, the above evidence appears to indicate that anti-PD-1 antibodies are capable of enhancing cytotoxic T cell activity toward PD-L1 overexpressing cells in vivo.

The instant claims are directed to a method for treatment of cancer, which implies an improvement in clinical outcome as the result of administration of anti-PD-1 antibody. In view of unpredictability of cancer therapy, as addressed in the previous office action, reliance solely on the experimental models disclosed in the specification is not seen as sufficient to enable one skilled in the art to practice "treatment" of cancer without undue experimentation, even if the disclosure is enabling for a method of enhancing cytotoxic T cell activity toward PD-L1 overexpressing cells in vivo, including in a cancer patient.

Applicant further argues that fully human antibodies, as recited in the amended claims, are less immunogenic in humans and are therefore less likely to be inactivated by the patient's immune system.

Applicant's argument is acknowledged, but is not seen as sufficient to overcome the rejection of record, for the reasons set forth supra.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended and newly added claims. The rejection of record is incorporated by reference herein, as if reiterated in full.

Applicant is invited to amend the claims to recite a method for enhancing cytotoxic T cell activity toward PD-L1 overexpressing cells, wherein the subject has cancer in order to overcome this rejection. Alternatively, Applicant is invited to present evidence predictive of positive clinical outcomes in cancer patients as the result of administering antibodies to PD-1.

4. The following is a quotation of the appropriate paragraphs of **35 U.S.C. 102** that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

*(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.*

5. Claims 13 and 14 stand rejected under **35 U.S.C. 102(e)** as being anticipated by Wood et al. (US Patent No. 6,808,710; see entire document), for the reasons of record.

Applicant's arguments have been fully considered but have not been found sufficiently convincing.

Applicant argues that Wood et al. do not teach completely human anti-PD-1 antibodies.

This is not found persuasive, because Wood et al. teach in Examples 9 and 10 (columns 80 – 81) fully human antibodies, including those against PD-1.

Applicant further argues that Wood et al. do not teach administering antibodies to a patient which cancer in which PD-L1 or PD-L2 are overexpressed.

This is not found sufficiently persuasive, because one of skill in the art at the time the invention was made would understand that treatment with anti-PD-1 antibodies cannot be effective against tumors which do not express PD-L1 or PD-L2. Therefore, one of skill in the art would understand that it is inherent in the teachings of Wood et al. that the antibody is administered to patients whose cancer cells express PD-L1 or PD-L1. It is noted that the instant claims do not specify any specific level of overexpression, nor a reference point; therefore, any level of PD-L1 or PD-L2 expression is within the scope of the instant claims.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection of record is incorporated by reference herein, as if reiterated in full.

***6. Conclusion: no claim is allowed.***

7. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is (571)272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ILIA OUSPENSKI, Ph.D./
Primary Examiner, Art Unit 1644
March 20, 2008